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NEWS	6	OCT 28	INPADOCDB/INPAFAMDB: Enhancements to the US national patent classification.
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NEWS	14	DEC 21	CAS Learning Solutions -- a new online training experience
NEWS	15	DEC 22	Value-Added Indexing Improves Access to World Traditional Medicine Patents in CAPLUS
NEWS	16	JAN 24	The new and enhanced DPCI file on STN has been released
NEWS	17	JAN 26	Improved Timeliness of CAS Indexing Adds Value to USPATFULL and USPAT2 Chemistry Patents
NEWS	18	JAN 26	Updated MeSH vocabulary, new structured abstracts, and other enhancements improve searching in STN reload of MEDLINE
NEWS	19	JAN 28	CABA will be updated weekly
NEWS	20	FEB 23	PCTFULL file on STN completely reloaded
NEWS	21	FEB 23	STN AnaVist Test Projects Now Available for Qualified Customers
NEWS	22	FEB 25	LPCI will be replaced by LDPCI
NEWS EXPRESS	17	DECEMBER 2010	CURRENT WINDOWS VERSION IS V8.4.2 .1, AND CURRENT DISCOVER FILE IS DATED 24 JANUARY 2011.
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FILE 'CAPLUS' ENTERED AT 21:24:18 ON 03 MAR 2011

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FILE COVERS 1907 - 3 Mar 2011 VOL 154 ISS 10

FILE LAST UPDATED: 2 Mar 2011 (20110302/ED)

REVISED CLASS FIELDS (/NCL) LAST RELOADED: Oct 2010

USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Oct 2010

Caplus now includes complete International Patent Classification (IPC) reclassification data for the fourth quarter of 2010.

CAS Information Use Policies apply and are available at:

<http://www.cas.org/legal/infopolicy.html>

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s flupirtine

L1 268 FLUPIRTINE

=> s l1 and neuropathic

9007 NEUROPATHIC

1 NEUROPATHICS

9007 NEUROPATHIC

(NEUROPATHIC OR NEUROPATHICS)

L2 18 L1 AND NEUROPATHIC

=> d l2 1-18 ibib ab

L2 ANSWER 1 OF 18 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2010:176183 CAPLUS

DOCUMENT NUMBER: 152:271166

TITLE: Crystalline forms of flupirtine

hydrochloride-maleic acid cocrystal

INVENTOR(S): Kalofonos, Isabel; Stahly, G. Patrick; Martin-Doyle,

William; Kalofonos, Dimitris; Stults, Jeffrey S.;

Hanko, Jason A.; Shipplett, Rex A.

PATENT ASSIGNEE(S): Bionevia Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 58pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2010017343	A2	20100211	WO 2009-US52925	20090806
WO 2010017343	A3	20100514		
W:	AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA			

PRIORITY APPLN. INFO.: US 2008-86644P P 20080806

AB The invention relates to crystalline forms of flupirtine, particularly to 1:1 flupirtine-HCl-maleic acid cocrystal. The preparation and characterization of 1:1 flupirtine hydrochloride-maleic acid cocrystal is described. The invention also relates to the therapeutic use of the flupirtine-HCl-maleic acid cocrystal to treat nervous system disorders, pain disorders, and musculoskeletal disorders and to pharmaceutical compns. containing the cocrystal.

L2 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2010:40881 CAPLUS

DOCUMENT NUMBER: 153:193645

TITLE: Tetrahydrocannabinol (delta 9-THC) treatment in

chronic central neuropathic pain and

fibromyalgia patients: results of a multicenter survey

AUTHOR(S): Weber, Janet; Schley, Marcus; Casutt, Matthias;

Gerber, Helmut; Schuepfer, Guido; Rukwied, Roman;

Schleinzner, Wolfgang; Ueberall, Michael; Konrad,

Christoph

CORPORATE SOURCE: Department of Anesthesiology, Intensive Care,

Emergency Medicine and Pain Therapy, Kantonsspital

Lucerne, Lucerne, 6000, Switz.

SOURCE: Anesthesiology Research and Practice (2009) No pp.

given

CODEN: ARPNCX; ISSN: 1687-6970

URL: <http://www.hindawi.com/journals/arp/contents.html>

PUBLISHER: Hindawi Publishing Corp.

DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English

AB Central neuropathic pain is difficult to treat, but delta 9-Tetrahydrocannabinol (delta 9-THC) may be a promising therapeutic agent. We administered in 172 patients on average 7.5 mg delta 9-THC over 7 mo. Of these, 48 patients prematurely withdrew due to side effects, insufficient analgesia, or expense of therapy. Thus, 124 patients were assessed retrospectively in a multicenter telephone survey. Reported changes in pain intensity, recorded on a numeric rating scale (NRS), Pain Disability Index (PDI), Medical Outcomes Short-Form (SF-12), Quality of Life Impairment by Pain (QLIP), Hospital Anxiety Depression Scale (HADS), and amount of concomitant pain medication were recorded. Psychometric parameters (PDI, SF-12, QLIP, HADS) and pain intensity improved significantly during delta 9-THC treatment. Opioid doses were reduced and patients perceived THC therapy as effective with tolerable side effects. About 25% of the patients, however, did not tolerate the treatment. Therapy success and tolerance can be assessed by a transient delta 9-THC titration and its maintained administration for several weeks. The present survey demonstrates its ameliorating potential for the treatment of chronic pain in central neuropathy and fibromyalgia. A supplemental delta 9-THC treatment as part of a broader pain management plan therefore may represent a promising coanalgesic therapeutic option.

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 3 OF 18 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2010:21671 CAPLUS

DOCUMENT NUMBER: 152:119669

TITLE: Preparation of benzoxazines, benzothiazines, and related compounds having NOS inhibitory activity for treatment of various diseases

INVENTOR(S): Ramnauth, Jailall; Annedi, Subhash C.; Silverman, Sarah; Dove, Peter; Maddaford, Shawn; Rakhit, Suman

PATENT ASSIGNEE(S): Neuraxon, Inc., Can.

SOURCE: PCT Int. Appl., 198pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2010000073	A1	20100107	WO 2009-CA923	20090703
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2009266386	A1	20100107	AU 2009-266386	20090703
CA 2729246	A1	20100107	CA 2009-2729246	20090703
AR 72471	A1	20100901	AR 2009-102506	20090703
US 20100009975	A1	20100114	US 2009-498185	20090706
PRIORITY APPLN. INFO.:			US 2008-133887P	P 20080703

## ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): MARPAT 152:119669

AB Disclosed are benzoxazines and benzothiazines of formula I (wherein Q = O-(CH<sub>2</sub>)<sub>1-3</sub>, S-(CH<sub>2</sub>)<sub>1-3</sub>, etc.; R<sub>1</sub> and R<sub>6</sub> = H, (un)substituted C<sub>1</sub>-6alkyl, C<sub>2</sub>-9heterocyclyl, etc.; R<sub>2</sub> and R<sub>3</sub> = H, halogen, (un)substituted C<sub>1</sub>-6alkyl, etc.; R<sub>4</sub> and R<sub>5</sub> is H, halogen, (CH<sub>2</sub>)NHC(NH)-(un)substituted C<sub>1</sub>-6alkyl, etc.; Y<sub>1</sub> and Y<sub>2</sub> = H, (un)substituted C<sub>1</sub>-6alkyl, or together are =O, etc.) having nitric oxide synthase (NOS) inhibitory activity, pharmaceutical and diagnostic compns. containing them, and their medical use, alone or in combination with other pharmaceutically agents, for the treatment or prevention of various medical conditions. Exemplary methods for synthesizing compds. of the invention were described, e.g., II was prepared by a multi-step synthesis involving nitro reduction of the corresponding benzoxazine followed by amidation with Me thiophene-2-carbimidothioate hydroiodide to give II. The invention compds. were found to exhibit selective inhibition of the neuronal isoform of NOS in in vitro inhibition assays, e.g., II demonstrated IC<sub>50</sub> value of 2.08  $\mu$ M for nNOS and 87.2  $\mu$ M for eNOS.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 4 OF 18 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2009:1460967 CAPLUS

DOCUMENT NUMBER: 151:558698

TITLE: Co-crystals of duloxetine and co-crystal formers for the treatment of pain

INVENTOR(S): Buschmann, Heimit Heinrich; Sola Carandell, Luis;

Benet Buchholz, Jordi; Ceron Bertran, Jordi Carles

PATENT ASSIGNEE(S): Laboratorios del Dr. Esteve S. A., Spain

SOURCE: Eur. Pat. Appl., 23pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 2123626	A1	20091125	EP 2008-384009	20080521
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, AL, BA, MK, RS				
CA 2724812	A1	20091126	CA 2009-2724812	20090520
WO 2009141144	A1	20091126	WO 2009-EP3617	20090520
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.: EP 2008-384009 A 20080521

WO 2009-EP3617 W 20090520

AB The present invention relates to co-crystals of duloxetine and co-crystal formers selected from active agents preferably with analgesic activity,

processes for preparation of the same and their uses as medicaments or in pharmaceutical formulations, more particularly for the treatment of pain.

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2009:1402799 CAPLUS

DOCUMENT NUMBER: 151:502914

TITLE: Methods and compositions for the management of pain using  $\omega$ -conotoxins

INVENTOR(S): Cooke, Ian; Goodchild, Colin Stanley

PATENT ASSIGNEE(S): CNSBio Pty. Ltd., Australia

SOURCE: PCT Int. Appl., 79pp.  
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2009135258	A1	20091112	WO 2009-AU563	20090506
W:	AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

PRIORITY APPLN. INFO.: US 2008-50869P P 20080506

AB The invention relates to the management of pain (nociceptive, neuropathic, inflammatory, and disease-related pain), using  $\omega$ -conotoxins alone or in combination with neuronal excitation inhibitors (analgesics). The invention in particular provides methods, protocols, compns. and devices which treat, alleviate, prevent, diminish, or otherwise ameliorate the sensation of pain.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2009:618978 CAPLUS

DOCUMENT NUMBER: 150:563641

TITLE: Preparation of indole compounds and methods for treating visceral pain and other conditions mediated by NOS or 5HT1D/1B receptors

INVENTOR(S): Maddaford, Shawn; Ramnauth, Jailall; Rakhit, Suman; Patman, Joanne; Renton, Paul; Annedi, Subhash C.; Andrews, John S.; Mladenova, Gabriela

PATENT ASSIGNEE(S): NeurAxon, Inc., Can.

SOURCE: PCT Int. Appl., 140pp.  
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2009062319	A1	20090522	WO 2008-CA2047	20081117
W:	AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
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AU 2008323526	A1	20090522	AU 2008-323526	20081117
CA 2705835	A1	20090522	CA 2008-2705835	20081117
US 20090192157	A1	20090730	US 2008-272775	20081117
EP 2220075	A1	20100825	EP 2008-850557	20081117
R:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, AL, BA, MK, RS			
KR 2010103799	A	20100928	KR 2010-7013312	20081117
CN 101910157	A	20101208	CN 2008-80124852	20081117
JP 2011503120	T	20110127	JP 2010-533403	20081117
MX 2010005342	A	20100809	MX 2010-5342	20100514
IN 2010DN04330	A	20101119	IN 2010-DN4330	20100616
PRIORITY APPLN. INFO.:			US 2007-988757P	P 20071116
			US 2008-133930P	P 20080703
			WO 2008-CA2047	W 20081117

## ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASREACT 150:563641; MARPAT 150:563641

AB The invention features methods of treating visceral pain or a condition in a mammal caused by the action of nitric oxide synthase (NOS) or by the action of serotonin 5HT1D/1B receptors, by administering to a patient in need thereof a therapeutically effective amount of an indole compound of Formula I (wherein R1 is H, (un)substituted C1-6 alkyl, (un)substituted C1-4 alkaryl, etc.; R2 and R3 are independently, H, halo, (un)substituted C1-6 alkyl, etc.; R4 and R7 are independently H, F, C1-6 alkyl, or C1-6 alkoxy; R5 is H, R5AC(NH)NH(CH2)r5, or R5BNHC(S)-NH(CH2)r5, wherein r5 is 0-2, R5A and R5B are, for example, (un)substituted C1-6 alkyl; R6 is H, F, R6AC(NH)NH(CH2)r6, or R6BNHC(S)-NH(CH2)r6, wherein r6 is 0-2, R6A and R6B are, for example, (un)substituted C1-6 alkyl), or a pharmaceutically acceptable salt or prodrug thereof. The methods of the invention may further comprise the administration of addnl. therapeutic agent. The invention also features new compds. of Formula I, pharmaceutical compns. thereof, and methods of resolving enantiomeric mixts. Example compound II enantiomers were prepared by reacting 3-(1-methylpyrrolidin-3-yl)-1H-indol-5-amine with benzyl chloroformate to form (+)-benzyl 3-(1-methylpyrrolidin-3-yl)-1H-indol-5-ylcarbamate; resolution of the enantiomers using chiral HPLC or SFC (supercrit. fluid chromatog.); deprotecting each enantiomer by hydrogenation and reacting each with thiophene-2-carbimidothioate. In an assay to measure selective inhibition of human NOS, II, (+)-II, and (-)-II showed selectivity for nNOS vs. eNOS or iNOS.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ACCESSION NUMBER: 2009:618035 CAPLUS  
 DOCUMENT NUMBER: 150:539562  
 TITLE: Preparation of 3,5-Substituted indole compounds having NOS and norepinephrine reuptake inhibitory activity  
 INVENTOR(S): Annedi, Subhash C.; Maddaford, Shawn; Ramnauth, Jailall; Renton, Paul; Rakhit, Suman; Andrews, John S.; Mladenova, Gabriela  
 PATENT ASSIGNEE(S): NeurAxon, Inc., Can.  
 SOURCE: PCT Int. Appl., 101pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2009062318	A1	20090522	WO 2008-CA2033	20081117
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
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US 20090131503	A1	20090521	US 2008-272656	20081117
CA 2705833	A1	20090522	CA 2008-2705833	20081117
EP 2220074	A1	20100825	EP 2008-848701	20081117
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MX 2010005343	A	20100809	MX 2010-5343	20100514
PRIORITY APPLN. INFO.:			US 2007-988741P	P 20071116
			US 2008-133975P	P 20080703
			WO 2008-CA2033	W 20081117

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASREACT 150:539562; MARPAT 150:539562

AB The present invention relates to novel 3,5-substituted indole compds. of Formula I (wherein R1 and R2 are independently, H, (un)substituted C1-6 alkyl, (un)substituted C3-8cycloalkyl, etc., or together form part of a ring; R3 is H, halo, (un)substituted C1-6 alkyl, etc.; R4, R6, and R7 are independently H, halo, C1-6 alkyl, or C1-6-alkoxy; R5 is R5AC(NH)NH(CH2)r5, wherein r5 is 0-2, R5A is, e.g., (un)substituted C1-6 alkyl; n is 0-2; m is 0-2) having nitric oxide synthase (NOS) inhibitory activity, particularly those that selectively inhibit neuronal nitric oxide synthase (nNOS) in preference to other eNOS isoforms. I also act as norepinephrine reuptake inhibitors. I, alone or in combination with other pharmaceutically active agents, can be used for treating or preventing conditions such as chronic pain and psychiatric disorders. Synthetic procedures for preparing I are exemplified. Example compound II was prepared in

7 steps from 5-nitroindole, 1,4-cyclohexanedione monoethylene acetal and Me thiophene-2-carbimidothioate hydroiodide. In bioassays measuring activity against human nNOS, eNOS, and NET, II had IC50 values of 0.49, 26.9, and 0.52  $\mu$ M.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD



(1 CITINGS)  
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2011 ACS on STN  
ACCESSION NUMBER: 2009:541573 CAPLUS  
DOCUMENT NUMBER: 151:69429  
TITLE: Neural KCNQ (Kv7) channels  
AUTHOR(S): Brown, David A.; Passmore, Gayle M.  
CORPORATE SOURCE: Department of Pharmacology, University College London,  
London, UK  
SOURCE: British Journal of Pharmacology (2009), 156(8),  
1185-1195  
CODEN: BJPCBM; ISSN: 1476-5381  
PUBLISHER: Wiley-Blackwell  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: English

AB A review. KCNQ genes encode five Kv7 K+ channel subunits (Kv7.1-Kv7.5).  
Four of these (Kv7.2-Kv7.5) are expressed in the nervous system, Kv7.2 and  
Kv7.3 are the principal mol. components of the slow voltage-gated  
M-channel, which widely regulates neuronal excitability, although other  
subunits may contribute to M-like currents in some locations. M-channels  
are closed by receptors coupled to Gq such as M1 and M3 muscarinic  
receptors; this increases neuronal excitability and underlies some forms  
of cholinergic excitation. Muscarinic closure results from activation of  
phospholipase C and consequent hydrolysis and depletion of membrane  
phosphatidylinositol-4,5-bisphosphate, which is required for channel  
opening. Some effects of M-channel closure, determined from transmitter  
action, selective blocking drugs (linopirdine and XE991) and KCNQ2 gene  
disruption or manipulation, are as follows: (i) in sympathetic neurons:  
facilitation of repetitive discharges and conversion from phasic to tonic  
firing; (ii) in sensory nociceptive systems: facilitation of A-delta  
peripheral sensory fiber responses to noxious heat; and (iii) in  
hippocampal pyramidal neurons: facilitation of repetitive discharges,  
enhanced after-depolarization and burst-firing, and induction of  
spontaneous firing through a reduction of action potential threshold at the  
axon initial segment. Several drugs including flupirtine and  
retigabine enhance neural Kv7/M-channel activity, principally through a  
hyperpolarizing shift in their voltage gating. In consequence they reduce  
neural excitability and can inhibit nociceptive stimulation and  
transmission. Flupirtine is in use as a central analgesic;  
retigabine is under clin. trial as a broad-spectrum anticonvulsant and is  
an effective analgesic in animal models of chronic inflammatory and  
neuropathic pain.

OS.CITING REF COUNT: 21 THERE ARE 21 CAPLUS RECORDS THAT CITE THIS  
RECORD (21 CITINGS)  
REFERENCE COUNT: 83 THERE ARE 83 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 9 OF 18 CAPLUS COPYRIGHT 2011 ACS on STN  
ACCESSION NUMBER: 2009:455187 CAPLUS  
DOCUMENT NUMBER: 150:431750  
TITLE: Pharmaceutical compositions containing benfotiamine  
and analgesics for the treatment of  
neuropathic pain  
INVENTOR(S): Bonke, Dieter; Medina-Santilla, Roberto; Reyes-Garcia,  
Gerardo  
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany  
SOURCE: PCT Int. Appl., 43pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent

LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2009046801	A1	20090416	WO 2008-EP7364	20080909
W:	AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
AU 2008310114	A1	20090416	AU 2008-310114	20080909
CA 2701838	A1	20090416	CA 2008-2701838	20080909
EP 2207569	A1	20100721	EP 2008-801937	20080909
R:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, AL, BA, MK, RS			
JP 2010540668	T	20101224	JP 2010-528285	20080909
US 20100279984	A1	20101104	US 2010-681424	20100712
PRIORITY APPLN. INFO.:			EP 2007-19693	A 20071009
			WO 2008-EP7364	W 20080909

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention relates to pharmaceutical compns. containing benfotiamine and one or more pharmaceutically active agents selected from the group consisting of analgesic acting substances selected from gabapentin, pregabalin, XP13512, carbamacepin, amitryptiline, ketorolac, diclofenac, ibuprofen, flurpiritin, paracetamol and dexamethasone, their preparation, and use for treatment and prevention of conditions and diseases consisting of pain conditions of neuropathic origin. Allodynic activity of a combination of gabapentin and benfotiamine is demonstrate in a neuropathic pain model in rats. Pharmaceutical compns. are also prepared

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 10 OF 18 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2009:179834 CAPLUS

DOCUMENT NUMBER: 150:222312

TITLE: Pharmaceutical synergistic compositions comprising dextromethorphan or other N-methyl-D-aspartate receptor antagonist, tramadol, and gabapentin, and possibly capsaicinoid, for treating chronic pain and pain associated with neuropathy

INVENTOR(S): Singh, Chandra U.

PATENT ASSIGNEE(S): Trinity Laboratories, Inc., USA

SOURCE: PCT Int. Appl., 116 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2009021058	A2	20090212	WO 2008-US72360	20080806
WO 2009021058	A3	20100114		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
EP 2184986	A2	20100519	EP 2008-782637	20080806
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, AL, BA, MK, RS				
JP 2010535802	T	20101125	JP 2010-520287	20080806
US 20110039875	A1	20110217	US 2010-452936	20100129
IN 2010MN00220	A	20100702	IN 2010-MN220	20100204
PRIORITY APPLN. INFO.:			US 2007-954251P	P 20070806
			WO 2008-US72360	W 20080806

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention provides methods and compns. for the treatment of neuropathic pain. In certain embodiments, compns. comprising an dextromethorphan (or other N-methyl-D-aspartate receptor antagonist), tramadol, and gabapentin can synergistically act to reduce pain in a human patient. Pharmaceutical compns. may also comprise a capsaicinoid, an esterified capsaicinoid, and/or a tricyclic antidepressant. Thus, capsule formulation comprised (in mg/capsule): tramadol hydrochloride 39.8, dextromethorphan hydrochloride 51.0, gabapentin 90.0, microcryst. cellulose 27.6, sodium lauryl sulfate 1.6.

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

L2 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2009:1412 CAPLUS

DOCUMENT NUMBER: 150:90558

TITLE: Combination methods and compositions for treatment of neuropathic pain

INVENTOR(S): Goodchild, Colin Stanley

PATENT ASSIGNEE(S): Cnsbio Pty Ltd, Australia

SOURCE: PCT Int. Appl., 86pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2009000038	A1	20081231	WO 2008-AU929	20080626
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU,  
IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK,  
TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD,  
TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW,  
AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

EP 2175886 A1 20100421 EP 2008-757008 20080626

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU,  
IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI,  
SK, TR, AL, BA, MK, RS

US 20100316678 A1 20101216 US 2010-666433 20100805

PRIORITY APPLN. INFO.: US 2007-946923P P 20070628

WO 2008-AU929 W 20080626

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention relates generally to the field of pain management,  
and in particular, the management of neuropathic pain. The  
present invention further provides methods and compns. that treat,  
alleviate, prevent, diminish or otherwise ameliorate the symptoms of  
neuropathic pain without inducing overt sedation. The present  
invention also contemplates combination therapy using one or more NK  
antagonists in combination with one or more compds. which decrease or  
inhibit neuronal excitation in the treatment of pain in association with the  
treatment of a particular disease condition or pathol.

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD  
(2 CITINGS)

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 12 OF 18 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2008:1368013 CAPLUS

DOCUMENT NUMBER: 149:541723

TITLE: Controlled-release flupirtine compositions,  
compacts, kits and methods of making and use thereof  
INVENTOR(S): Terhaag, Bernd; Qadan, Asal; Wolf, Joachim; Faustmann,  
Barbara

PATENT ASSIGNEE(S): AWD.pharma GmbH & Co. KG, Germany

SOURCE: U.S. Pat. Appl. Publ., 18 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20080279930	A1	20081113	US 2007-745374	20070507
US 20080279952	A1	20081113	US 2007-840917	20070817

PRIORITY APPLN. INFO.: US 2007-745374 A1 20070507

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention relates to compns. and compacts comprising  
flupirtine or a pharmaceutically acceptable salt thereof in which  
there is controlled-release of at least a portion of flupirtine  
or a pharmaceutically acceptable salt thereof. The invention further  
relates to kits comprising such compns. and compacts, and methods of  
making and using such compns. and compacts.

L2 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2008:1155351 CAPLUS

DOCUMENT NUMBER: 149:402219

TITLE: Preparation of tetrahydroquinolines and related  
compounds having NOS inhibitory activity

INVENTOR(S): Maddaford, Shawn; Ramnauth, Jailall; Rakhit, Suman;

PATENT ASSIGNEE(S): Patman, Joanne; Annedi, Subhash C.; Andrews, John; Dove, Peter; Silverman, Sarah; Renton, Paul  
 SOURCE: Neuraxon, Inc., Can.  
 U.S. Pat. Appl. Publ., 148 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20080234237	A1	20080925	US 2008-54083	20080324
AU 2008232269	A1	20081002	AU 2008-232269	20080325
CA 2681771	A1	20081002	CA 2008-2681771	20080325
WO 2008116308	A1	20081002	WO 2008-CA569	20080325
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AR 65845	A1	20090708	AR 2008-101216	20080325
EP 2139886	A1	20100106	EP 2008-748081	20080325
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR				
JP 2010521527	T	20100624	JP 2010-500037	20080325
MX 2009010193	A	20091215	MX 2009-10193	20090923
IN 2009DN06796	A	20100625	IN 2009-DN6796	20091023
CN 101679397	A	20100324	CN 2008-80017025	20091123
PRIORITY APPLN. INFO.:			US 2007-896829P	P 20070323
			WO 2008-CA569	W 20080325

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): MARPAT 149:402219

AB The invention features quinolones, tetrahydroquinolines, and related compds. with the formula I that inhibit nitric oxide synthase (NOS), particularly those that selectively inhibit neuronal nitric oxide synthase (nNOS) in preference to other NOS isoforms. Compds. with the formula I [Q= (CHR<sub>6</sub>)<sub>n</sub>, where n = 1-3; R<sub>1</sub> and each R<sub>6</sub> independently = H, (un)substituted alkyl, alkaryl, alkheterocyclyl or heterocyclyl; R<sub>2</sub> and R<sub>3</sub> independently = H, (un)substituted alkyl, aryl, alkaryl, heterocyclyl, alkoxy, thioalkoxy, etc.; R<sub>4</sub> and R<sub>5</sub> independently = H, (CH<sub>2</sub>)<sub>m</sub>NHC(NH)R<sub>6</sub>, or (CH<sub>2</sub>)<sub>m</sub>NHC(S)NHR<sub>6</sub>; m = 0-2; R<sub>6</sub> = (un)substituted alkyl, aryl, alkaryl, heterocyclyl, alkheterocyclyl, etc.; Y<sub>1</sub> and Y<sub>2</sub> independently = H, alkyl, aryl, alkaryl, heterocyclyl, hydroxy, alkoxy, thioalkoxy or alkheterocyclyl; or Y<sub>1</sub> and Y<sub>2</sub> together = O], and their pharmaceutically acceptable salts or prodrugs, are prepared and disclosed. Thus, e.g., II was prepared by nitration of 3,4-dihydro-2(1H)-quinoline followed by alkylation with 2-(N,N-dimethylamino)ethyl chloride hydrochloride, nitro reduction and amidation with Me thiophene-2-carbimidothioate hydroiodide to give II. I have been found to exhibit selective inhibition of the neuronal isoform of NOS in in vitro inhibition assays, e.g., II demonstrated IC<sub>50</sub> value of 0.58 μM for nNOS and 41.1 μM for eNOS. The NOS inhibitors of the invention, alone or in combination with other

pharmaceutically active agents, can be used for treating or preventing various medical conditions.

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD  
(2 CITINGS)

L2 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2008:7807 CAPLUS  
DOCUMENT NUMBER: 148:106186  
TITLE: Polymorphic forms of flupirtine maleate  
PATENT ASSIGNEE(S): Pliva Istrazivanje I Rezvoi d.o.o., Croatia  
SOURCE: Ger. Gebrauchsmusterschrift, 21pp.  
CODEN: GGXXFR  
DOCUMENT TYPE: Patent  
LANGUAGE: German  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 202007011042	U1	20080103	DE 2007-202007011042	20070712
DE 102007032612	A1	20080124	DE 2007-102007032612	20070712
CA 2657541	A1	20080117	CA 2007-2657541	20070713
WO 2008007117	A1	20080117	WO 2007-GB2647	20070713
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
EP 2046749	A1	20090415	EP 2007-766224	20070713
R:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS			
IN 2009DN00700	A	20090522	IN 2009-DN700	20090129
CN 101506169	A	20090812	CN 2007-80030827	20090219
PRIORITY APPLN. INFO.:			GB 2006-13928	A 20060713
			DE 2007-102007032612A	20070712
			WO 2007-GB2647	W 20070713

AB The invention concerns novel polymorphic forms of flupirtine maleate with characteristic x-ray powder diffraction pattern and differential scanning calorimetry curve. The polymorphic forms excel with increased efficiency as non-narcotic, centrally acting analgesics. No formulation example is given.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD  
(1 CITINGS)

L2 ANSWER 15 OF 18 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2007:1285926 CAPLUS  
DOCUMENT NUMBER: 148:417721  
TITLE: Antihyperalgesic and analgesic properties of the N-methyl-D-aspartate (NMDA) receptor antagonist neramexane in a human surrogate model of neurogenic hyperalgesia  
AUTHOR(S): Klein, Thomas; Magerl, Walter; Hanschmann, Angelika; Althaus, Michael; Treede, Rolf-Detlef

CORPORATE SOURCE: Institute of Physiology and Pathophysiology, Johannes  
Gutenberg University, Mainz, D-55099, Germany  
SOURCE: European Journal of Pain (Amsterdam, Netherlands)  
(2007), Volume Date 2008, 12(1), 17-29  
CODEN: EJPAFJ; ISSN: 1090-3801  
PUBLISHER: Elsevier B.V.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB NMDA-receptors are a major target in the prevention and treatment of hyperalgesic pain states in neuropathic pain. However, previous studies revealed equivocal results depending on study design and efficacy parameters. We tested the analgesic (generalized reduction of generation and processing of nociceptive signalling) and anti-hyperalgesic (prevention of central sensitization) properties of the NMDA-receptor antagonist neramexane and the potassium channel opener flupirtine in the intradermal capsaicin injection model. Furthermore, we tested the effect on pain summation (wind up). Eighteen healthy subjects received either a single dose of neramexane (40 mg p.o.), flupirtine (100 mg) or placebo in a double-blind, randomized, cross-over study. Pain evoked by intradermal capsaicin injection as well as pain evoked by pinpricks was significantly reduced by neramexane (-22% to -30% vs. placebo) in the non-sensitized skin indicating a marked analgesic effect. Moreover, dynamic mech. allodynia (pain to light touch) was also significantly attenuated by neramexane (-28% vs. placebo). However, static secondary hyperalgesia to pinprick stimuli after capsaicin injection was not significantly reduced (-9% vs. placebo). Flupirtine showed no analgesic or anti-hyperalgesic effect. Mech.-evoked wind up of pain sensation was not affected by any treatment. The results suggests that in a human surrogate model of neurogenic hyperalgesia a single low-dose of neramexane had a marked analgesic effect in the sensitized and in the non-sensitized state and thus may be a useful drug to treat the enhanced pain sensitivity in neuropathic pain patients. Its efficacy may be based on analgesia rather than anti-hyperalgesia or anti-windup. In contrast, flupirtine showed neither an analgesic nor an anti-hyperalgesic effect at a dose used for the treatment of postoperative pain.

OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD  
(6 CITINGS)

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 16 OF 18 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2006:1204362 CAPLUS

DOCUMENT NUMBER: 145:505331

TITLE: Substituted indole compounds having NOS inhibitory  
activity and their preparation and pharmaceutical  
composition

INVENTOR(S): Maddaford, Shawn; Ramnauth, Jailall; Rakhit, Suman;  
Patman, Joanne; Renton, Paul; Annedi, Subhash C.

PATENT ASSIGNEE(S): Neuraxon, Inc., Can.

SOURCE: U.S. Pat. Appl. Publ., 129 pp.  
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20060258721	A1	20061116	US 2006-404267	20060413
US 7375219	B2	20080520		

AU 2006321284	A1	20070607	AU 2006-321284	20060413
CA 2605073	A1	20070607	CA 2006-2605073	20060413
WO 2007063418	A2	20070607	WO 2006-IB3873	20060413
WO 2007063418	A3	20071221		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
EP 1883451	A2	20080206	EP 2006-831851	20060413
EP 1883451	B1	20101124		
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
JP 2008535908	T	20080904	JP 2008-505999	20060413
ZA 2007009038	A	20090128	ZA 2007-9038	20060413
BR 2006007517	A2	20090908	BR 2006-7517	20060413
NZ 563191	A	20091127	NZ 2006-563191	20060413
AT 489138	T	20101215	AT 2006-831851	20060413
AR 55053	A1	20070801	AR 2006-101505	20060417
MX 2007012818	A	20080114	MX 2007-12818	20071015
NO 2007005632	A	20080111	NO 2007-5632	20071106
KR 2008021596	A	20080307	KR 2007-7026397	20071113
IN 2007CN05128	A	20080627	IN 2007-CN5128	20071113
CN 101247853	A	20080820	CN 2006-80020788	20071211
US 20080249302	A1	20081009	US 2008-47963	20080313
PRIORITY APPLN. INFO.:			US 2005-670856P	P 20050413
			US 2006-404267	A1 20060413
			WO 2006-IB3873	W 20060413

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): MARPAT 145:505331

AB The invention features compds. of formula I as inhibitors of nitric oxide synthase (NOS), particularly those that selectively inhibit neuronal nitric oxide synthase (nNOS) in preference to other NOS isoforms. The NOS inhibitors of the invention, alone or in combination with other pharmaceutically active agents, can be used for treating or preventing conditions such as, for example, stroke, reperfusion injury, neurodegeneration, head trauma, CABG, migraine headache with and without aura, migraine with allodynia, central post-stroke pain (CPSP), neuropathic pain, morphine/opioid induced tolerance and hyperalgesia. Compds. of formula I wherein R1 is H, (un)substituted C1-6 alkyl, (un)substituted C1-4 alkylaryl, and (un)substituted C1-4 alkylheterocyclyl; R2 and R3 are independently H, halo, (un)substituted C1-6 alkyl, (un)substituted C6-10 aryl, (un)substituted C1-4 alkylaryl, (un)substituted C2-9 bridge heterocyclyl, etc.; R4 and R7 are independently H, F, C1-6 alkyl, and C1-6 alkoxy; R5 is H, R5AC(NH)NH(CH2)r, and R5ANHC(S)NH(CH2)r; r is an integer from 0 to 2; R5A is (un)substituted C1-6 alkyl, (un)substituted C6-10 aryl; (un)substituted C1-4 alkylaryl, etc.; R6 is H, R6AC(NH)(CH2)r and R6ANHC(S)(CH2)r; R6A is equal to R5A; and their pharmaceutically acceptable salts and prodrugs thereof are claimed. Example compound II was prepared by N-alkylation of 6-nitroindole with N,N-dimethyl-2-chloroethylamine; the resulting N-(2-dimethylaminoethyl)-6-nitroindole underwent reduction to give the corresponding 6-aminoindole derivative, which underwent addition to



thiophene-2-carboximidothionic acid Ph ester hydrobromide to give compound II. All the invention compds. were evaluated for their NOS inhibitory activity. From the assay, it was determined that compound II exhibited IC50 values of 8.8  $\mu$ M against Rat nNOS, 109  $\mu$ M against Murine iNOS, 211  $\mu$ M against Bovine eNOS, 1.2  $\mu$ M against Human nNOS, 60  $\mu$ M against Human iNOS and 15  $\mu$ M against Human eNOS.

OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)

L2 ANSWER 17 OF 18 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2005:564580 CAPLUS

DOCUMENT NUMBER: 143:83486

TITLE: Flupirtine compositions for treatment of neuropathic or inflammatory pain treatment

INVENTOR(S): Nadeson, Raymond; Tucker, Adam Paul; Goodchild, Colin

PATENT ASSIGNEE(S): Monash University, Australia

SOURCE: PCT Int. Appl., 93 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005058319	A1	20050630	WO 2004-AU1772	20041216
W:				
AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW:				
BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004298288	A1	20050630	AU 2004-298288	20041216
CA 2550023	A1	20050630	CA 2004-2550023	20041216
EP 1701725	A1	20060920	EP 2004-802074	20041216
R:				
AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
CN 1917876	A	20070221	CN 2004-80041741	20041216
JP 2007513981	T	20070531	JP 2006-544174	20041216
NZ 547926	A	20091030	NZ 2004-547926	20041216
IN 2006DN03996	A	20070824	IN 2006-DN3996	20060711
US 20080039463	A1	20080214	US 2007-574438	20070625
PRIORITY APPLN. INFO.:			AU 2003-906981	A 20031216
			WO 2004-AU1772	W 20041216

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Compns. of flupirtine for management of neuropathic or inflammatory pain optionally including 1 or more analgesics including opiates, NSAIDS and other active agents in immediate and controlled release forms. Methods and systems for administration of these compns. Nonsedative doses of flupirtine can increase the antinociception following morphine without causing sedation.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 18 OF 18 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2003:933608 CAPLUS  
DOCUMENT NUMBER: 140:399049  
TITLE: The therapeutic potential of neuronal KCNQ channel modulators  
AUTHOR(S): Gribkoff, Valentin K.  
CORPORATE SOURCE: Department 401, Neuroscience Drug Discovery, Bristol-Myers Squibb Pharmaceutical Research Institute, Wallingford, CT, 06492, USA  
SOURCE: Expert Opinion on Therapeutic Targets (2003), 7(6), 737-748  
CODEN: EOTTAO; ISSN: 1472-8222  
PUBLISHER: Ashley Publications Ltd.  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: English

AB A review. Neuronal KCNQ (Kv7) channels (KCNQ2 - 5 or Kv7.2 - 7.5, disclosed to date) were discovered by virtue of their homol. with a known cardiac channel involved in long QT syndrome (KvLQT or KCNQ1, Kv7.1) and first disclosed in 1998. The involvement of KCNQ2 (Kv7.2) and KCNQ3 (Kv7.3) in a benign idiopathic neonatal epilepsy, KCNQ4 (Kv7.4) in a form of congenital deafness, and the discovery that neuronal KCNQ heteromultimers were among the mol. substrates of M-channels, resulted in a high level of interest for potential drug development strategies. A number of small-mol. modulators were quickly identified, including openers or activators such as the antiepileptic drug candidate retigabine and the structurally-related analgesic drug flupirtine, and a group of KCNQ channel inhibitors/blockers originally developed for cognition enhancement. All of these data have suggested a rich target profile for modulators of neuronal KCNQ channels, including a variety of neuronal hyperexcitability disorders and conditions for openers, such as the epilepsies, acute pain, neuropathic pain, migraine pain and some neurodegenerative and psychiatric disorders. KCNQ blockers could likewise have utility in disorders characterized by neuronal hypoactivity, including cognition enhancement and perhaps disorders of mood. Emerging patent literature suggests significant interest in neuronal KCNQ modulation in the pharmaceutical industry and significant chemical diversity concerning KCNQ modulation.

OS.CITING REF COUNT: 42 THERE ARE 42 CAPLUS RECORDS THAT CITE THIS RECORD (42 CITINGS)  
REFERENCE COUNT: 100 THERE ARE 100 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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COST IN U.S. DOLLARS  
FULL ESTIMATED COST

SINCE FILE	TOTAL
ENTRY	SESSION
64.40	66.93

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)  
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SINCE FILE	TOTAL
ENTRY	SESSION
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FULL ESTIMATED COST	3.36	70.29

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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)		
CA SUBSCRIBER PRICE	0.00	-15.66

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FILE COVERS 1907 - 3 Mar 2011 VOL 154 ISS 10  
FILE LAST UPDATED: 2 Mar 2011 (20110302/ED)  
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Oct 2010  
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Oct 2010

Caplus now includes complete International Patent Classification (IPC) reclassification data for the fourth quarter of 2010.

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<http://www.cas.org/legal/infopolicy.html>

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=> file reg  
COST IN U.S. DOLLARS

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FULL ESTIMATED COST	4.68	74.97

	SINCE FILE ENTRY	TOTAL SESSION
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)		
CA SUBSCRIBER PRICE	0.00	-15.66

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STRUCTURE FILE UPDATES: 2 MAR 2011 HIGHEST RN 1265968-43-1  
DICTIONARY FILE UPDATES: 2 MAR 2011 HIGHEST RN 1265968-43-1

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<http://www.cas.org/support/stngen/stndoc/properties.html>

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L3           STRUCTURE UPLOADED

=> s ll sss full

L4           4 FLUPIRTINE

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	6.21	81.18
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-15.66

FILE 'CAPLUS' ENTERED AT 21:57:56 ON 03 MAR 2011  
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FILE COVERS 1907 - 3 Mar 2011 VOL 154 ISS 10  
FILE LAST UPDATED: 2 Mar 2011 (20110302/ED)  
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Oct 2010  
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Oct 2010

Caplus now includes complete International Patent Classification (IPC) reclassification data for the fourth quarter of 2010.

CAS Information Use Policies apply and are available at:

<http://www.cas.org/legal/infopolicy.html>

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 14  
L5 252 L4

=> s 14 and pain  
252 L4  
83928 PAIN  
2159 PAINS  
85295 PAIN  
(PAIN OR PAINS)  
L6 62 L4 AND PAIN

=> s 16 and py<2004  
24052889 PY<2004  
L7 17 L6 AND PY<2004

=> d 17 1-17 ibib ab

L7 ANSWER 1 OF 17 CAPLUS COPYRIGHT 2011 ACS on STN  
ACCESSION NUMBER: 2005:1246751 CAPLUS  
DOCUMENT NUMBER: 144:16985  
TITLE: Investigation of flupirtine in comparison with  
analgesic and sedative agents in a feline thermal  
pain model  
AUTHOR(S): Spiecker-Hauser, Ute  
CORPORATE SOURCE: Germany  
SOURCE: (2003) No pp. given Avail.: Metadata on  
Internet Documents, Order No. 48932  
From: Metadata Internet Doc. [Ger. Diss.] 2003,  
(D1007-4), No pp. given  
URL: <http://www.meind.de/search.py?recid=48932>  
DOCUMENT TYPE: Dissertation  
LANGUAGE: German  
AB Unavailable

L7 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2011 ACS on STN  
ACCESSION NUMBER: 2003:625345 CAPLUS  
DOCUMENT NUMBER: 139:345808  
TITLE: Analgesic efficacy of flupirtine in primary care of  
patients with osteoporosis related pain: A  
multivariate analysis  
AUTHOR(S): Ringe, Johann D.; Miethe, Dirk; Pittrow, David;  
Wegscheider, Karl  
CORPORATE SOURCE: Medical Clinic IV, Leverkusen Medical Center,  
University of Cologne, Cologne, Germany  
SOURCE: Arzneimittel-Forschung (2003), 53(7),  
496-502  
CODEN: ARZNAD; ISSN: 0004-4172  
PUBLISHER: Editio Cantor Verlag  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB Although chronic pain in elderly patients with osteoporosis is  
extremely common it has rarely been addressed in pharmacotherapy studies.  
The efficacy and tolerability of flupirtine (CAS 56995-20-1,  
Trancopal Dolo) up to 600 mg/day was investigated under daily practice  
conditions. This was an open-label, multicenter, prospective,  
observational phase IV study on 869 patients performed in 290 practices  
(mainly orthopedists) throughout Germany. Decrease in pain  
scores on a visual analog scale (VAS, from 0 = none to 10 = maximum) after an  
average 3-wk therapy, and evaluation of adverse events. Multivariate analyses  
were performed to identify factors associated with the efficacy of  
pain reduction 81% Of patients were female; the mean age of all

patients was 67 yr, and the mean body mass index was 25.7 kg/m<sup>2</sup>. 81% Of patients had reduced bone d., 30% had a family history of osteoporosis, and 32% had previous bone fractures. The mean daily flupirtine dose was 270±12 mg. The mean baseline pain VAS scores were 7.1 (low back pain), 5.8 (neck pain), 5.6 (shoulder-arm pain), and 6.6 (other pain). Mean pain reduction at the end of flupirtine treatment was 43% for low back pain, 44% for neck pain, 40% for shoulder-arm pain, and 40% for other pain (all redns. p < 0.05 vs. baseline). Rates of pain reduction at the various sites were closely correlated, and the efficacy of pain reduction was independent of age. The pain reduction was more pronounced in patients with recent onset of pain and with higher pain intensity at entry. Tolerability of treatment was excellent with only 2.4% of patients reporting adverse events and only 12 patients (1.4%) withdrawing from the trial. This trial performed under daily practice conditions in a large unselected sample of patients confirms the efficacy and safety of flupirtine in the treatment of chronic pain in patients with osteoporosis, independent of the age of the patient.

OS.CITING REF COUNT: 9 THERE ARE 9 CAPLUS RECORDS THAT CITE THIS RECORD (9 CITINGS)

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2001:100977 CAPLUS

DOCUMENT NUMBER: 134:141760

TITLE: Use of flupirtine for alleviating pain caused by degenerative joint diseases in dogs and cats

INVENTOR(S): Endler, Gabriele; Lehmann, Holger; Lobisch, Michael; Szelenyi, Istvan

PATENT ASSIGNEE(S): Asta Medica AG, Germany; Bayer AG

SOURCE: PCT Int. Appl., 20 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2001008682	A2	20010208	WO 2000-EP7356	20000729 <--
WO 2001008682	A3	20020718		
W: AU, BG, BR, BY, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, UZ, YU, ZA				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
BR 2000012942	A	20020709	BR 2000-12942	20000729 <--
EP 1242078	A2	20020925	EP 2000-960383	20000729 <--
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HU 2003001296	A2	20030828	HU 2003-1296	20000729 <--
JP 2003530308	T	20031014	JP 2001-513412	20000729 <--
CA 2314746	A1	20010203	CA 2000-2314746	20000801 <--
NO 2002000364	A	20020123	NO 2002-364	20020123 <--
MX 2002000997	A	20031014	MX 2002-997	20020129 <--
ZA 2002000493	A	20030225	ZA 2002-493	20020221 <--
HR 2002000192	A2	20040229	HR 2002-192	20020301
PRIORITY APPLN. INFO.:			US 1999-147033P	P 19990803
			WO 2000-EP7356	W 20000729

AB Flupirtine, or a pharmaceutically acceptable salt thereof, is used for treating pain caused by degenerative joint diseases that can be accompanied by inflammation in dogs and cats. The inventive substances are also used to prevent such pain from becoming chronic.

OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2000:725448 CAPLUS

DOCUMENT NUMBER: 133:276364

TITLE: Flupirtine in the treatment of fibromyalgia and related conditions

INVENTOR(S): Stoll, Andrew L.

PATENT ASSIGNEE(S): USA

SOURCE: PCT Int. Appl., 15 pp.  
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000059487	A2	20001012	WO 2000-US6446	20000405 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 20020018809	A1	20020214	US 2000-534325	20000324 <--
US 6610324	B2	20030826		
CA 2366865	A1	20001012	CA 2000-2366865	20000405 <--
EP 1169040	A2	20020109	EP 2000-921384	20000405 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002541097	T	20021203	JP 2000-609051	20000405 <--
PRIORITY APPLN. INFO.:				
			US 1999-128141P	P 19990407
			US 2000-534325	A 20000324
			WO 2000-US6446	W 20000405

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention is directed to a method for treating the symptoms associated with fibromyalgia and related conditions by administering flupirtine.

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

L7 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 1999:98939 CAPLUS

DOCUMENT NUMBER: 130:320252

TITLE: The intracutaneous pain model in the assessment of analgesic efficacy

AUTHOR(S): Scharein, Eckehard; Bromm, Burkhardt

CORPORATE SOURCE: Institute for Physiology, University Hospital Eppendorf, Hamburg, D-20246, Germany

SOURCE: Pain Reviews (1998), 5(4), 216-246  
CODEN: PAREFV; ISSN: 0968-1302

PUBLISHER: Arnold, Hodder Headline PLC  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: English

AB This review, with 164 refs., summarizes the results of studies using the intracutaneous pain model in the assessment of nociceptive information transfer from cutaneous afferents to pain-relevant cortical structures, as measured by spontaneous and stimulus-evoked electroencephalog. activity. The application of multivariate statistical analyses, such as principal component anal., on the late brain potentials, results in the identification of two pain-related principal components with loading maxima around 150 and 250 ms after stimulation, which vary with the reported painfulness of the stimulus. The application of pain-related evoked cerebral potentials in studies of pain-relieving drugs makes possible a quant. comparison of their analgesic potency. The drugs tested were acetaminophen, phenazone, acetylsalicylic acid, ibuprofen, anpirtoline, diclofenac, denaverine, flupirtine, imipramine, meperidine, naloxone, pentazocine, tilidine and tramadol, several of them in different dosages and formulations. The interstudy comparison revealed that there was a high correlation ( $r = 0.91$ ) between pain relief at the subjective measurement level and a decrease in pain-related brain potentials.

OS.CITING REF COUNT: 10 THERE ARE 10 CAPLUS RECORDS THAT CITE THIS RECORD (10 CITINGS)

REFERENCE COUNT: 164 THERE ARE 164 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 1998:727904 CAPLUS

DOCUMENT NUMBER: 130:90441

TITLE: Antioxidant properties of the triaminopyridine, flupirtine

AUTHOR(S): Gassen, Michael; Pergande, Gabriela; Youdim, Moussa B. H.

CORPORATE SOURCE: DEPARTMENT OF PHARMACOLOGY, EVE TOPF AND NATIONAL PARKINSON'S FOUNDATION CENTERS, BRUCE RAPPAPORT FAMILY RESEARCH INSTITUTE, FACULTY OF MEDICINE, HAIFA, 31096, Israel

SOURCE: Biochemical Pharmacology (1998), 56(10), 1323-1329

CODEN: BCPA6; ISSN: 0006-2952

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Flupirtine is a triaminopyridine-derived centrally acting analgesic, which interacts with mechanisms of noradrenergic pain modulation. Recently, it has been found to display neuroprotective effects in various models of excitotoxic cell damage, global and focal ischemia. Although this profile suggests that flupirtine acts as an antagonist of the N-methyl-D-aspartate (NMDA) and glutamate-triggered  $\text{Ca}^{2+}$  channel, there is no direct interaction with the receptor. In this paper, we examined whether flupirtine can act as an antioxidant and prevent free radical-mediated structural damage. Flupirtine at 5-30  $\mu\text{M}$  inhibited ascorbate/ $\text{Fe}^{2+}$  (1-10  $\mu\text{M}$ )-stimulated formation of thiobarbituric reactive substances, an indicator of lipid peroxidn., in rat brain mitochondria. Interestingly, we found an increasing effectiveness of the drug at higher iron concns. Addnl., higher concns. of flupirtine also provided protection against protein oxidation, as demonstrated by a decrease in protein carbonyls formed after treatment of rat brain homogenates with ascorbate/ $\text{Fe}^{2+}$ . In PC12 cell culture, flupirtine at 10-100  $\mu\text{M}$  was able to attenuate  $\text{H}_2\text{O}_2$ -stimulated cell death and improve the survival by 33%.



OS.CITING REF COUNT: 13 THERE ARE 13 CAPLUS RECORDS THAT CITE THIS  
RECORD (13 CITINGS)  
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2011 ACS on STN  
ACCESSION NUMBER: 1997:369751 CAPLUS  
DOCUMENT NUMBER: 126:347309  
ORIGINAL REFERENCE NO.: 126:67457a,67460a  
TITLE: Analgesic immediate and controlled release  
pharmaceutical composition  
INVENTOR(S): Smith, Ian Keith; Heinicke, Grant Wayne  
PATENT ASSIGNEE(S): F.H. Faulding & Co. Limited, Australia  
SOURCE: PCT Int. Appl., 35 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9714415	A1	19970424	WO 1996-AU658	19961018 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG				
CA 2235071	A1	19970424	CA 1996-2235071	19961018 <--
AU 9672078	A	19970507	AU 1996-72078	19961018 <--
AU 708408	B2	19990805		
EP 858334	A1	19980819	EP 1996-933279	19961018 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6194000	B1	20010227	US 1998-62060	19980417 <--
PRIORITY APPLN. INFO.:			AU 1995-6057	A 19951019
			WO 1996-AU658	W 19961018

# ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB A pharmaceutical composition for use in the treatment (also preemptively) of chronic or acute pain contains an NMDA receptor antagonist in an immediate-release form in association with an NMDA receptor antagonist in a controlled-release form. The NMDA receptor antagonist may be selected from a morphinan such as dextromethorphan and dextrorphan, ketamine, amantadine, memantine, eliprodil, ifenprodil, dizocilpine, remacemide, lamotrigine, riluzole, aptiganel, phencyclidine, flupirtine, celfotel, felbamate, spermine, spermidine, levemopamil, or a pharmaceutically acceptable salt, ester, or metabolic precursor thereof. Thus, capsules were filled with a blend of immediate-release dextromethorphan cores and controlled-release dextromethorphan coated pellets in a ratio of 25:75, where the pellets were coated with a solution containing di-Et phthalate 0.65, methacrylic acid copolymer 1.05, ethylcellulose N50 3.59, PEG-6000 1.28, and 96% EtOH 93.43 weight%. The capsules released 26.7% of their dextromethorphan content in 0.5 h and 82.0% in 12 h.

OS.CITING REF COUNT: 22 THERE ARE 22 CAPLUS RECORDS THAT CITE THIS  
RECORD (23 CITINGS)  
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2011 ACS on STN  
ACCESSION NUMBER: 1994:426878 CAPLUS

DOCUMENT NUMBER: 121:26878  
ORIGINAL REFERENCE NO.: 121:4733a,4736a  
TITLE: Pharmaceutical composition consisting of flupirtine and morphine for the treatment of pain and to avoid a morphine addiction  
INVENTOR(S): Nickel, Bernd; Lobisch, Michael; Szelenyi, Stefan; Engel, Juergen; Emig, Peter; Pergande, Gabriela  
PATENT ASSIGNEE(S): ASTA Medica AG, Germany  
SOURCE: Eur. Pat. Appl., 10 pp.  
CODEN: EPXXDW  
DOCUMENT TYPE: Patent  
LANGUAGE: German  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 595311	A1	19940504	EP 1993-117472	19931028 <--
EP 595311	B1	19970122		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
DE 4236752	A1	19940505	DE 1992-4236752	19921030 <--
US 5521178	A	19960528	US 1993-141678	19931027 <--
AT 147979	T	19970215	AT 1993-117472	19931028 <--
ES 2099344	T3	19970516	ES 1993-117472	19931028 <--
CA 2102072	A1	19940501	CA 1993-2102072	19931029 <--
CA 2102072	C	20050104		
BR 9304431	A	19940607	BR 1993-4431	19931029 <--
JP 06211663	A	19940802	JP 1993-271730	19931029 <--
JP 3665354	B2	20050629		
HU 66085	A2	19940928	HU 1993-3089	19931029 <--
HU 219907	B	20010928		

PRIORITY APPLN. INFO.: DE 1992-4236752 A 19921030

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Coadministration of flupirtine and morphine results in additive analgesic activity, reduced dependence on morphine, and no development of tolerance to flupirtine. Thus, the excitation, rearing behavior, and rigidity seen in rats after withdrawal from morphine in long-term expts. were markedly less in rats which had been injected with morphine and flupirtine. A preferred dosage form was a tablet containing 50-500 mg flupirtine and 10-250 mg morphine as salts.

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

L7 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 1993:462262 CAPLUS

DOCUMENT NUMBER: 119:62262

ORIGINAL REFERENCE NO.: 119:10977a,10980a

TITLE: Flupirtine: a review of its pharmacological properties, and therapeutic efficacy in pain states

AUTHOR(S): Friedel, Heather A.; Fitton, Andrew

CORPORATE SOURCE: Adis Int. Ltd., Auckland, N. Z.

SOURCE: Drugs (1993), 45(4), 548-69  
CODEN: DRUGAY; ISSN: 0012-6667

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with many refs. Flupirtine is a novel nonopiate centrally acting analgesic agent with muscle relaxant properties, advocated for use in a number of pain states. Preliminary evidence suggests that flupirtine 100 to 200 mg orally or 150 mg rectally 3 to 4 times daily (maximum daily dose 600 mg) is more effective than placebo in relieving

moderate acute pain of various types. For the relief of pain due to surgery, traumatic injury, dental procedures, headache/migraine and abdominal spasms, flupirtine has proved at least as effective as the opiate analgesics codeine, dihydrocodeine and pentazocine, the nonsteroidal antiinflammatory agents suprofen, diclofenac and ketoprofen, as well as dipyrene and paracetamol (acetaminophen). Although evidence to support a role in the treatment of chronic pain is limited, flupirtine has been found as effective as pentazocine in short term trials of patients with muscular or neuralgiform pain, dysmenorrhea, soft tissue rheumatism or cancer pain. The safety profile of flupirtine has not yet been fully established, although initial evidence suggests that adverse reactions, while frequent, are usually minor in nature. The most common reactions are drowsiness, dizziness, dry mouth and various gastrointestinal complaints. In comparison with opiate drugs, flupirtine appears to produce fewer central nervous system effects, no respiratory or cardiovascular depression, and no overt tolerance or phys. dependence on prolonged administration. If these initially favorable results are confirmed in larger long term trials, then flupirtine would appear to represent an effective analgesic for the relief of moderate pain, particularly that of musculoskeletal origin.

OS.CITING REF COUNT: 51 THERE ARE 51 CAPLUS RECORDS THAT CITE THIS RECORD (51 CITINGS)

L7 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 1991:485346 CAPLUS  
DOCUMENT NUMBER: 115:85346  
ORIGINAL REFERENCE NO.: 115:14495a,14498a  
TITLE: Dose-related analgesic effects of flupirtine  
AUTHOR(S): Hummel, T.; Friedmann, T.; Pauli, E.; Niebch, G.;  
Borbe, H. O.; Kobal, G.  
CORPORATE SOURCE: Dep. Pharmacol. Toxicol., Univ. Erlangen-Nuernberg,  
Erlangen, W-8520, Germany  
SOURCE: British Journal of Clinical Pharmacology (1991  
, 32(1), 69-76  
CODEN: BCPHBM; ISSN: 0306-5251  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Flupirtine is a novel and, in all probability, centrally acting, analgesic. The present investigation was conducted in order to investigate dose-related effects of perorally administered flupirtine in man, with special regard to specifically analgesic actions, employing a model based on pain-related chemosomatosensory evoked potentials and subjective intensity ests. of painful stimuli. Plasma concns. of flupirtine measured 2 h after dosing linearly increased as a function of the administered dose. It was possible to reproduce the results obtained by the authors previously, which established the analgesic action of 200 mg flupirtine administered perorally. Intensity ests. linearly decreased as a function of the administered dose, whereas chemosomatosensory evoked potential amplitudes non-linearly changed in relation to the administered dose. In the spontaneous EEG, a dose-dependent increment in the power-spectra was observed, and this mainly in the alpha- and beta-range.

OS.CITING REF COUNT: 9 THERE ARE 9 CAPLUS RECORDS THAT CITE THIS RECORD (9 CITINGS)

L7 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 1989:470889 CAPLUS  
DOCUMENT NUMBER: 111:70889  
ORIGINAL REFERENCE NO.: 111:11791a,11794a  
TITLE: Mode of antinociceptive action of flupirtine in the rat

AUTHOR(S): Szelenyi, I.; Nickel, B.; Borbe, H. O.; Brune, K.  
CORPORATE SOURCE: Dep. Pharmacol., ASTA Pharma A.-G., Frankfurt/Main,  
D-6000, Fed. Rep. Ger.  
SOURCE: British Journal of Pharmacology (1989),  
97(3), 835-42  
CODEN: BJPCBM; ISSN: 0007-1188

DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Flupirtine is a novel, centrally acting, nonopioid analgesic agent. The present investigation was undertaken to ascertain which neuronal systems might be responsible for its antinociceptive effect in rodents. The antinociceptive responses to test compds. were examined in the tail-flick test. The selective destruction of noradrenergic pathways by 6-hydroxydopamine considerably reduced the flupirtine-induced inhibition of nociceptive responses but clonidine-induced antinociception was enhanced. Depletion of spinal 5-hydroxytryptaminergic pathways by pretreatment with 5,7-dihydroxytryptamine failed to affect the action of flupirtine and clonidine. The depletion of neurotransmitters by reserpine totally abolished the antinociceptive action of flupirtine. By contrast, clonidine-induced inhibition of nociceptive responses remained unchanged. Inhibition of the synthesis of noradrenaline by  $\alpha$ -methyl-L-p-tyrosine attenuated the antinociception induced by flupirtine. In contrast, inhibition of the synthesis of 5-hydroxytryptamine by ( $\pm$ )-6-fluorotryptophan did not influence the antinociceptive activity of flupirtine. Inhibition of noradrenaline uptake by imipramine augmented flupirtine-induced antinociception. Selective antagonists at  $\alpha$ -adrenoceptors decreased the antinociceptive action of flupirtine. Antinociception induced by clonidine was diminished by idazoxan but not by prazosin. The 5-hydroxytryptamine antagonist ketanserin diminished the antinociceptive activity of flupirtine, probably due to its addnl.  $\alpha$ 1-adrenoceptor antagonist activity. The antinociceptive effect of clonidine was not influenced by ketanserin. Cholinoceptor antagonists such as mecamylamine and pirenzepine did not alter the antinociceptive action of flupirtine. Flupirtine-induced antinociception also remained unchanged after pretreatment with haloperidol. Flupirtine had no pharmacol. relevant affinity for  $\alpha$ 1- or  $\alpha$ 2-adrenoceptors or 5-HT1- and 5-HT2-receptors in direct binding studies. Thus, the antinociceptive action induced by flupirtine depends on the descending noradrenergic pain-modulating system.

OS.CITING REF COUNT: 19 THERE ARE 19 CAPLUS RECORDS THAT CITE THIS  
RECORD (19 CITINGS)

L7 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 1988:486279 CAPLUS  
DOCUMENT NUMBER: 109:86279  
ORIGINAL REFERENCE NO.: 109:14243a,14246a  
TITLE: Flupirtine depresses nociceptive activity evoked in  
rat thalamus  
AUTHOR(S): Bleyer, Hannelore; Carlsson, Karl Heinz; Erkel, Hans  
Juergen; Jurna, Ilmar  
CORPORATE SOURCE: Inst. Pharmakol. Toxikol., Univ. Saarlandes,  
Homburg/Saar, 6650, Fed. Rep. Ger.  
SOURCE: European Journal of Pharmacology (1988),  
151(2), 259-65  
CODEN: EJPHAZ; ISSN: 0014-2999  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Flupirtine, a novel analgesic agent, was tested on nociceptive activity in neurons of the dorsomedial part of the ventral nucleus of the thalamus (VDM) and ascending axons of the spinal cord of rats under urethane

anesthesia. Activity was elicited by supramaximal stimulation of the sural nerve. Flupirtine injected i.v. dose dependently reduced nociceptive activity in the thalamus and ascending axons. The ED50 of flupirtine in depressing the thalamic response was 1.9 mg/kg, and the ED50 in depressing the C fiber-evoked response in ascending axons was 18 mg/kg. Naloxone reduced the depression of the nociceptive response evoked in the thalamus when applied before but not when applied after flupirtine. The results indicate that flupirtine produces analgesia by spinal inhibition of nociceptive impulse transmission from afferent nerve fibers to neurons sending their axons to the brain and, in addition, by supraspinal inhibition of nociceptive impulse transmission to the thalamus. Opioid mechanisms could be involved in these effects.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD  
(1 CITINGS)

L7 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 1988:68813 CAPLUS  
DOCUMENT NUMBER: 108:68813  
ORIGINAL REFERENCE NO.: 108:11247a,11250a  
TITLE: Effects of flupirtine on the pain-related  
evoked potential and the spontaneous EEG  
AUTHOR(S): Kobal, G.; Hummel, T.  
CORPORATE SOURCE: Dep. Pharmacol. Toxicol., Univ. Erlangen-Nuernberg,  
Erlangen, D-8520, Fed. Rep. Ger.  
SOURCE: Agents and Actions (1988), 23(1-2), 117-19  
CODEN: AGACBH; ISSN: 0065-4299  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB The analgesic activity of flupirtine in humans was evident at 30-60 min and maximal at 1.5-2 h. Flupirtine decreased the EEG response to painful stimuli, but did not affect acoustic evoked potentials. The drug also increased the power d. in all frequency bands of the spontaneous EEG. Flupirtine may affect the evaluation of painful stimuli, but not the conduction of nociceptive activity.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD  
(1 CITINGS)

L7 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 1988:68812 CAPLUS  
DOCUMENT NUMBER: 108:68812  
ORIGINAL REFERENCE NO.: 108:11247a,11250a  
TITLE: Possible involvement of noradrenergic descending  
pain-modulating pathways in the mode of  
antinociceptive action of flupirtine, a novel  
non-opioid analgesic  
AUTHOR(S): Nickel, B.; Engel, J.; Szelenyi, I.  
CORPORATE SOURCE: Dep. Pharmacol., Asta Pharm A.-G., Frankfurt/Main,  
D-6000, Fed. Rep. Ger.  
SOURCE: Agents and Actions (1988), 23(1-2), 112-16  
CODEN: AGACBH; ISSN: 0065-4299  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Flupirtine dose-dependently increased pain threshold in the electrostimulated pain test in mice. Its antinociceptive activity was attenuated by simultaneous administration of the noradrenergic  $\alpha 1/\alpha 2$ -antagonist yohimbine and the  $\alpha 2$ -antagonist idazoxane. By contrast, the analgesia induced by codeine or morphine was not influenced by  $\alpha 2$ -adrenergic antagonists at all. A striking resemblance could be observed in the pharmaco-EEG of freely moving rats treated with clonidine and flupirtine, resp. The noradrenergic descending pain-modulating system might be

involved in the antinociceptive mode of action of flupirtine.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD  
(1 CITINGS)

L7 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 1988:31754 CAPLUS

DOCUMENT NUMBER: 108:31754

ORIGINAL REFERENCE NO.: 108:5181a,5184a

TITLE: Effect of flupirtine maleate on the nociceptive pathway, EEG, evoked potentials and polysynaptic reflexes in laboratory animals

AUTHOR(S): Gordon, R.; Sofia, R. Duane; Diamantis, W.

CORPORATE SOURCE: Dep. Pharmacol., Wallace Lab., Cranbury, NJ, 08512, USA

SOURCE: Postgraduate Medical Journal, Supplement (1987), 63(3), 49-55

CODEN: PMESAJ; ISSN: 0370-0593

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Flupirtine maleate (3, 6, or 10 mg/kg, i.v.) elevated the pain threshold following elec. stimulation of rabbit tooth pulp with a peak effect at 10 min. Codeine (1, 3, or 6 mg/kg, i.v.), but not zomepirac (3, 6, or 10 mg/kg, i.v.), was also effective. In the cat elec. stimulation of the tooth pulp or the contralateral sciatic nerve (central and peripheral nociceptive pathways, resp.) resulted in evoked potentials (activation) in the midbrain (MRF), thalamus (VPL) and sensory cortex. Flupirtine maleate (1 mg/kg, i.v.) did not alter the evoked responses. However, at 3 and 6 mg/kg, i.v. it effectively blocked activation in the MRF, VPL and sensory cortex, primarily following tooth pulp stimulation rather than after sciatic nerve stimulation, suggesting that flupirtine was a selective antagonist of the central nociceptive pathway. Furthermore, in the cat, flupirtine at 3 mg/kg, i.v., blocked cortical and hippocampal arousal (activation) following MRF stimulation. At 6 and 10 mg/kg it partially antagonized the linguomandibular reflex (central polysynaptic reflex), but had little or no effect on the flexor reflex (peripheral polysynaptic reflex).

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD  
(1 CITINGS)

L7 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 1988:31750 CAPLUS

DOCUMENT NUMBER: 108:31750

ORIGINAL REFERENCE NO.: 108:5181a,5184a

TITLE: The antinociceptive activity of flupirtine: a structurally new analgesic

AUTHOR(S): Nickel, B.

CORPORATE SOURCE: Biol. Res. Pharmacol., Homburg Degussa Pharma Gruppe, Frankfurt, D-6000/1, Fed. Rep. Ger.

SOURCE: Postgraduate Medical Journal, Supplement (1987), 63(3), 19-28

CODEN: PMESAJ; ISSN: 0370-0593

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In the electrostimulated pain test in mice the oral ED50 for flupirtine was 25.7 mg/kg. Thus, flupirtine was .apprx.31.7 times more potent than paracetamol and as potent as pentazocine. Morphine was 1.5 times and buprenorphine 9.9 times more potent than flupirtine. In the hot plate test in mice, flupirtine (ED50: 32 mg/kg) was .apprx.1/2 as potent as morphine. The oral and i.v. antinociceptive activity of flupirtine in the elec. tooth pulp stimulation test in conscious dogs was 3.5 mg/kg, orally, and 0.7 mg/kg, i.v., which was similar to that of pentazocine.

Buprenorphine had, as expected, stronger antinociceptive activity. Fifteen min after oral administration of 40 mg flupirtine/kg, the pain threshold in the electrostimulated pain test was increased by 54%. The maximal antinociceptive effect was observed 30 min after dosing. The analgesia lasted  $\geq 75$  min. Codeine elevated the pain threshold 15 min after dosing. Its maximal effect was also reached 30 min after application, but the antinociceptive activity wore off earlier than after flupirtine. The intracerebroventricular and intrathecal administration of flupirtine also caused dose-dependent analgesia in dose ranges which, when applied systemically, did not produced analgesia in rats. The antinociceptive activity of flupirtine was not abolished by naloxone whether given orally or by the intraventricular or intrathecal routes. In opiate receptor binding studies flupirtine had no affinity for  $\mu$ -,  $\delta$ -, or  $\kappa$ -opiate receptors of the highest concentration used ( $10^{-5}$ M). Whereas buprenorphine and tramadol showed a striking similarity in the pharmaco-EEG recorded from different parts of the brain (frontal cortex, thalamus, striatum and the mesencephalic reticular formation) of the freely moving rat, flupirtine was clearly different in action. It produced dose-dependent increases in nearly all frequency bands, but its effects were different from those of the minor tranquilizer diazepam and the anticonvulsant phenobarbital. Apparently, the central antinociceptive activity of flupirtine is not based on an opiate mechanism and is not comparable with that of diazepam and phenobarbital.

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD  
(2 CITINGS)

L7 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 1985:143132 CAPLUS

DOCUMENT NUMBER: 102:143132

ORIGINAL REFERENCE NO.: 102:22339a,22342a

TITLE: Studies on the pharmacological activity of flupirtine, a structurally new analgesic

AUTHOR(S): Jakovlev, V.; Sofia, R. D.; Achterrath-Tuckermann, U.; Von Schlichtegroll, A.; Thiemer, K.

CORPORATE SOURCE: Chemiewerk Homburg, Degussa A.-G., Frankfurt/Main, D-6000, Fed. Rep. Ger.

SOURCE: Arzneimittel-Forschung (1985), 35(1), 30-43  
CODEN: ARZNAD; ISSN: 0004-4172

DOCUMENT TYPE: Journal

LANGUAGE: German

AB The analgesic potency of flupirtine (I) [56995-20-1] in mice and rats in Haffner's test, electropain test, and Randall-Selitto test (inflammation-induced pain) lies between the more potent dextromoramide and methadone and the more weakly active pethidine, dextropropoxyphene codeine, phenacetin, and paracetamol. I is enterally absorbed to a higher degree than the other tested centrally acting analgesics. The duration of action of I is comparable to that of codeine. I exhibits a distinct central analgesic component of action, with no signs of opiate properties. As seen in rat paw edemas and in adjuvant arthritis, I has a peripheral antiinflammatory component of action. Because the antiinflammatory doses of I are higher than the analgesic EDs and the inhibition of prostaglandin biosynthesis by I is observed only in higher concns., its antiinflammatory activity observed in animals can hardly be expected in humans. Ulcerogenic effects, occurring often after strong antiinflammatory agents, have not been found after I. In contrast to opiates and other strong acting analgesics I shows an antipyretic activity in the yeast fever test in rats, which is comparable to that of phenacetin. This activity was not observed in human studies.

OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD  
(3 CITINGS)

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